UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/349,489	12/02/1994	DAVID B. RING	0999.001	6479

7590 09/10/2004

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/349,489	RING, DAVID B.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 6/14/2004 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-3, 8 and 15 are pending and examined on the merits.

4. For clarification of the record, it is noted that in the previous Office action, a rejection of claims 1-3, 8 and 15 under U.S.C. 103(a) as being unpatentable over Hsieh-Ma et al, Weiner et al, or Ring, in view of Fanger et al, or Snider et al., and further in view of Ring (US. Patent 6,054,561) was withdrawn. In the previous Office action, this rejection was listed under "Claim Rejections Withdrawn", but the examiner inadvertently typed "maintained" instead of "withdrawn" in the statement setting forth the status of the claims.

Claim Rejections Withdrawn:

5. The rejections of claims 1-3, and 15 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods comprising the administration of bispecific antibodies comprising a first binding site that binds to FcγRIII and a second binding site that binds to the antigens c-erbB-2, HMW mucin, HMW mucin II, p-glycoprotein, does not reasonably provide enablement for methods comprising the administration of bispecific

antibodies comprising a first binding site that binds to FcγRIII and a second binding site that binds to an antigen that is solely characterized as an antigen that binds to a monoclonal antibody produced by a hybridoma cell, is withdrawn. The amendment to the claims appears to limit the binding of the second antigen binding site to antigens selected from the group c-erbB-2, HMW mucin, HMW mucin II, and p-glycoprotein.

Claim Rejections Maintained:

6. The rejection of claims 1-3 under 35 U.S.C. 102(e) as being anticipated by Ring (U.S. Patent 5,959,084; issued Sep. 29, 1999; effective filing date Oct. 29, 1990) is maintained for the reasons of record.

Applicant's arguments have been carefully considered, but fail to persuade. Applicant asserts that because Ring fails to specifically state that the methods of disclosed in the '084 patent result in production of antibodies, that Ring fails to teach each and every element of the claimed methods. This argument is not persuasive because applicant has failed to show that the amount of bispecific antibody used in Ring is different from an amount of bispecific antibody that would be sufficient to kill cancer cells. As discussed in the previous Office action, Ring teaches bispecific antibodies that bind to FcγRIII and to p-glycoprotein, and methods of administering bispecific antibodies to patients (col. 24, line 63 – col. 25, line 24). Because the instant specification fails to teach that the amounts of bispecific antibodies that would be sufficient to produce antibodies in a patient are different from the amounts that would be sufficient to kill cancer cells when injected in a patient, it is assumed that because the steps of the claimed methods are the same as those of Ring's methods (administration of a bispecific

antibody within the scope of bispecific antibodies recited in the claims), that the methods of Ring inherently result in the production of antibodies. Thus, Ring teaches methods that are the same as that claimed because Ring teaches a method comprising the same active steps of the claimed methods (i.e. same antibody, same step of administering to a patient).

7. The rejection of claims 1-3 and 8 under 35 U.S.C. 102(b) as being anticipated by Weiner (Weiner, L.M. et al. Cancer Res. 53: 94-100, 1993, Jan. 1; previously cited) is maintained for the reasons of record.

Applicant's arguments have been carefully considered, but fail to persuade. Applicant asserts that because Weiner fails to specifically state that the methods of disclosed in Weiner result in production of antibodies, that Weiner fails to teach each and every element of the claimed methods. This argument is not persuasive because applicant has failed to show that the amounts of bispecific antibody used in Weiner is different from the amounts of antibodies that result in the induction of antibody production against a cancer antigen. As discussed in the previous Office action, Weiner teaches a method of administering the 2B1 bispecific antibody (and how to make the 2B1 bispecific antibody (see reference 20)), to scid mice that have been injected with peripheral blood lymphocytes (PBL) (see page 97, 2nd col. – page 98, bridging paragraph). Thus, Weiner teaches the methods as claimed, because the Weiner's method step is the same as the method step of the claimed invention (administration of a bispecific antibody). Because the scid mice (which read on "patients") were also injected with PBL, the method of Weiner would inherently result in the production of antibodies. Thus, Weiner teaches the methods as claimed.

8. The rejection of claim 15 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for the reasons of record. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Because claim 15 is directed to methods where the bispecific antibody is administered to a patient not expressing the antigen to which the second binding site binds, the method of claim 15 reads on a prophylactic methods of tumor vaccination, and would require administration of the bispecific antibody prior to the development of tumors.

Applicant's arguments have been carefully considered, but are not persuasive. Applicant asserts that claim 15 does not read on a prophylactic method of tumor vaccination, and therefore, that the claimed method is fully enabled by the specification. This argument is not found persuasive, because the specification teaches that (page 8, lines 3-7) "the term "patient" refers to a mammal capable of expressing FcγRIII on the surface of cells, the mammal being presently afflicted with *or potentially afflicted with* any number of disease treatable by the method of the invention" (emphasis added). The specification teaches that the diseases include cancer. Because claim 15 is directed to administering a bispecific antibody to a patient, and the specification defines patient as a mammal afflicted with, or potentially afflicted with, a disease such as cancer, and further, the claim recites that the second antigen (a cancer antigen) is not present in the patient upon first administration, the claimed inventions clearly read on prophylactic methods of treating cancer. Therefore, the rejection is maintained for the reasons of record.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

The claimed methods are broadly drawn to methods of preventing cancer by administering a bispecific antibody prior to the development of tumors. The specification provides working examples for the treatment of tumors already present in a patient, where the bispecific antibody comprises a second binding site that binds to an antigen expressed by the tumor. However, the specification lacks any working examples to demonstrating the administration of a bispecific antibody to individuals not yet having cancer. Therefore, the specification contains no guidance for determining the appropriate time prior to the development of tumors to begin the therapy, or for identifying patients at risk for developing those tumors. In view of the above, one of skill in the art would be forced into undue experimentation for the purpose of determining appropriate times, and for identifying patients at risk. Therefore, one of skill in the art would not have a reasonable expectation of success in the practice of the claimed invention.

9. The rejection of claims 1-3 and 15 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. New grounds of rejection, which are necessitated by the amendment, are presented.

The basis of this rejection is that the amendment directed to the nature of the second binding site of the bispecific antibodies used in the claimed methods is not supported by the specification as originally filed.

The amendment to claim 1 results in the characterization of the second binding site of the bispecific antibody to be a second binding site capable of recognizing and binding a second antigen, where the second antigen is selected from the goup consisting of c-erbB-2, HMW mucin, HMW mucin II and p-glycoprotein, and further that the second binding site comprises a binding sit derived from a monoclonal antibody produced by the list of hybridomas in claim 1.

The specification does not support this characterization of the second binding site because the specification defines (as applicant has pointed to in the response to the previous Office action) the term "binding site derived from a monoclonal antibody" as meaning a binding site in a second antibody or antibody fragment having the same or homologous CDRs as the monoclonal antibody. Homologous CDRs should be understood to include one set of CDRs from an antibody in which the primary sequence of each CDR is at least 50% identical to the antibody and the binding sit formed by these CDRs binds to the same epitope as the monoclonal antibody. The specification does not teach how to make or the structure of a second binding site, that for example, both binds to c-erbB-2 and is derived from antibody HB11830, which is a monoclonal antibody that binds to an uncharacterized 145 kD cancer antigen. In view of the definition in the specification where the second binding site must bind to the same epitope as the

antibody from which it was derived, and in view of the lack of teachings concerning the specific epitopes of each of the named monoclonal antibodies, it appears that an antibody binding site derived from a monoclonal antibody such as HB 11830 (that does not appear to bind to c-erbB-2, HMW mucin, HMW mucin II or p-glycoprotein) would not bind to any of the cancer antigens listed in the claim. Therefore, the claimed methods are not supported by the specification as originally filed.

Applicant is advised that one way to overcome this rejection is to delete the references to monoclonal antibodies that do not bind c-erbB-2, HMW mucin, HMW mucin II, or p-glycoprotein. The antibodies that do not appear to bind to these antigens are the following: HB 11830, HB 10802, HB 8490, HB 8485, HB 8691, HB 11052, HB 10812, HB 11769, HB 8486, HB 10789, HB 8488, HB 8662, HB 8697, HB 10785, HB 10796, HB 10798, HB 11768, HB 10793, HB 11752, HB 10795, HB 10801, HB 11751, HB 10794.

New Grounds of Rejection:

10. Claims 1-3 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the characterization of the second binding site of the bispecific antibody is unclear. As discussed above, the amendment limited the second antigen that binds to the second binding site of the bispecific antibody to c-erbB-2, HMW mucin, HMW mucin II or p-glycoprotein, where the second bind site is further characterized as comprising a binding site derived from a list of monoclonal antibodies that include monoclonal antibodies that

do not bind to any of c-erbB-2, HMW mucin, HMW mucin II and p-glycoprotein. Given the definition provided in the specification that derivation of a binding site from a monoclonal antibody includes the requirement that the binding site bind to the same epitope as the original monoclonal antibody, including monoclonal antibodies that do not bind to any of c-erbB-2, HMW mucin, HMW mucin II and p-glycoprotein in the list from which the binding site may derived renders the claim indefinite.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran
Patent Examiner
September 2, 2004

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
9/7/2004